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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/043,658	01/09/2002	Eric N. Olson	MYOG:024USC1	7444

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/043,658	**Applicant(s)** OLSON, ERIC N.	
	Examiner Joseph T. Woitach	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *12 September 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,4 and 9*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☒ Other: See Continuation Sheet.

Joel Woitach
AU 1632

Continuation of 11. does NOT place the application in condition for allowance because:

Examiner agrees in part with the summary by Applicant's of the two main issues raised in the enablement rejection under 35 USC 112, first paragraph. Specifically, first, Examiner would agree that there is insufficient evidence of record that one of skill in the art would correlate the observations of MEF2C with other forms of MEF2 known in the art, however further would maintain that because of the complexity of the process and hypertrophic affect there is question that simply affecting MEF2 would result in a method of treatment. Examiner has acknowledged on the record that MEF2 does participate in the signalling pathways used during the hypertrophy, however has provided sound scientific arguments supported by cited references for the complexity of the hypertrophic process and of signalling during this process wherein one of skill in the art would not have reasonably expected to practice the invention as claimed by simply affecting MEF2 function. Moreover, while forms of MEF2 may have similar functions in other systems, there is no evidence in the specification that anything besides MEF2C participates in the signalling pathway during hypertrophy. Moreover, the detailed analysis provided in the specification provides further evidence of the complexity and reliance of factors other than MEF2C in the signalling pathway during hypertrophy. Given this evidence one of skill in the art would not expect that trying to affect other isofroms would treat or be of any benefit in the claimed method. Applicant points to and cites Xu et al. arguing that their conclusion clearly supports MEF2 as a target and supports Applicant's position of declaritory evidence. This is not found persuasive because as Examiner has acknowledged that MEF2 signalling is observed during hypertrophy, even this citation states that the proof-of-principle is "potentially in association with a primary alteration in a subset....". More specfically, in light of the phenotypes of transgenic animals overexpressing MEF developing hypertrophy, one conlcude from the total teachings in Xu et al. that MEF2 is at best a primary response which results in a cascade of changes leading to hypertrophy. Once the cascade and consequent affect is present in a subject, there is no link nor post-filing evidence that affecting MEF2 would stop the consequences of the cascade, i.e. treat hypertrophy. Moreover, Xu et al. provide in vitro data demonstrating that MEF alone is not sufficient to induce hypertrophy in vitro, and the role and requirement other factors (bridging pages 6-7) clearly indicating the complexity of the process. Furthermore, the teachings of Xu et al in total must be considered, not general lines out of context, as one of skill in the art would. In this case, the skilled artisan would view would not consider MEF to be a target, and clearly in vitro it appears to play no role in hypertrophy (noting that that broadly claim 1 encompasses an in vitro embodiment of affecting a cardiomyocyte cell). An analogy can be made to the biology in cancer where an aberant gene or gene expression results in cancer formation, for example v-myc or ras expression models, however targeting these early factors that may trigger a cause are not effective targets once the transformation process to cancer has been established. As here, the evidence of record clearly indicates that overexpression of MEF can lead to hypertrophy in transgenic models, not in vitro as evidenced by Xu et al, however a myriad of factors are present and required for the end effect in a subject, where MEF is at best an initial signalling event not a protein that by itself causes the hypertrophy.

Secondly, with respect to methods required to practice the claimed invention, Examiner has acknowledged that working examples are not required, and would agree that specific guidance would not be required for methodology that is routine in the art. However, in this case, the methods relied upon for practicing the claimed invention as broadly claimed are not even clearly set forth in the claim nor the specification. Very importantly, no specific compounds are provided in the specification, nor is there any guidance to an end target except to the simplistic requirement that MEF2 function, any function, be affected, wherein this presumably results in treatment. The means and goal to this end are completely prophetic as evidenced by Example 5 of the specification (see page 77 of the specification). This is not a general secondary portion of the rejection because to practice the method as broadly claimed, the specific materials needed to predictably practice the method as broadly claimed should be provided to provide at least a starting point for the skilled artisan. In this case, there is no indication that praciticing the claimed method would use materials and/or methods known in the art, and to the contrary there is no art on the novelty indicating that such methods are known. Claim 9 recites using an anti-sense construct, however this is not a routine art accepted method, additionally noting that there is no guidance to what this construct would physically or functionally be, or how to effectively deliver a construct at therapeutic levels-or what a therapeutic level would even be as a target of reasonable experimentation. This is not a genealized dispersion or a requirement of efficacy of gene therapy as argued by Applicant (see page 4 of Applicant's amendment), rather it is a necessity of satisfying the requirements of 35 USC 112, first paragraph, for the claimed method. The argument of the office is not a general one, rather it builds on the problems specifically associated with the hypothesis on which the claimed invention is based. It is again noted that besides the general proposal to use an anti-sense construct, and even then there is no specific teaching of the materials or the methods in the specification for one of skill in the art. It is noted that the courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in patent application.

Continuation of 13. Other:

As noted by Applicant, page 3, section I, the claims still encompass more than the elected invention. Linking claim practice was used in the restriction requirement, and election was made without traverse--however at this time neither the linking claim nor claims drawn to the specific elected invention have been found allowable. The objection to the claims is maintained for the reasons of record.

It is noted that linking claim 1 is rather broad encompassing a method of treating cardiac hypertrophy, where the only active method step simply requires inhibiting the function of MEF2 without any specific indication of how this is done or specific outcome of what the method of treatment expect to treat or affect. The broadest reasonable interpretation of this claim allows for affecting MEF2 function by any means, even secondary affects of known methodology known and used in treating hypertrophy. While it may have not been explicitly examinerd or appreciated in the prior art, affecting MEF2 function would be anticipated by methods of treatment known in the art that would have inherently had this affect. A similar line of logic applies to claim 4 as well. Since the linking claim is rejected as it is drawn to the elected invention, and based on the broadest reasonable interpretation of the claim would be anticipated by known methods of treatingcardiac hypertrophy, the objection to the claims would be maintained.